Enhanced and preferential internalization of lipid nanocapsules into human glioblastoma cells: effect of a surface-functionalizing NFL peptide

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Increasing intracellular drug concentration using nanocarriers can be a potential strategy to improve efficacy against glioblastoma (GBM). Here, the fluorescent-labelled NFL-TBS·40-63 peptide (fluoNFL) concentration on a lipid nanocapsule (LNC) was studied to enhance nanovector internalization into human GBM cells. LNC surface-functionalization with various fluoNFL concentrations was performed by adsorption. LNC size and surface charge altered gradually with increasing peptide concentration, but their complement protein consumption remained low. Desorption of fluoNFL from the LNC surface was found to be slow. Furthermore, it was observed that the rate and extent of LNC internalization in the U87MG human glioblastoma cells were dependent on the surface-functionalizing fluoNFL concentration. In addition, we showed that the uptake of fluoNFL-functionalized LNCs was preferential towards U87MG cells compared to healthy human astrocytes. The fluoNFL-functionalized LNC internalization into the U87MG cells was energy-dependent and occurred possibly by macropinocytosis and clathrin-mediated and caveolin-mediated endocytosis. A new ferrocifen-type molecule (FcTriOH), as a potent anticancer candidate, was then encapsulated in the LNCs and the functionalization improved its in vitro efficacy compared to other tested formulations against U87MG cells. In the preliminary study, on subcutaneous human GBM tumor model in nude mice, a significant reduction of relative tumor volume was observed at one week after the second intravenous injection with FcTriOH-loaded LNCs. These results showed that enhancing NFL peptide concentration on the LNC surface is a promising approach for increased and preferential nanocarrier internalization into human GBM cells, and the FcTriOH-loaded LNCs are a promising therapy approach for GBM.

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